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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,661	05/07/2002	Dan L. Eaton	P3230R1C001-168	6201

30313 7590 01/11/2005

KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
IRVINE, CA 92614

EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,661	EATON ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/17/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to comply & App.A*.

DETAILED ACTION

1. Applicant's preliminary amendment filed on 10 September 2002 is acknowledged and entered. Claims 1-13 are pending and under consideration. The claims are drawn to the protein designated PRO1926, also identified as encoded by DNA82340-2530 and ATCC accession number 203547, shown in Figures 135 (nucleic acid) and 136 (protein).

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). **Applicant is required to provide a paper copy of the CRF in response to the Office Action.**

Drawings

4. The Office acknowledges the receipt of the drawings filed 5/7/2002.

Information Disclosure Statement

5. The information disclosure statement, filed 9/17/2002 has been considered. The BLAST results demonstrate that applicants are aware of polypeptide with

identity/homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the Examiner cannot determine if said sequences constitute prior art.

Priority Determination

6. The claimed polypeptide has no utility, see rejection below. Since no utility is disclosed in the priority applications they aren't enabling under 35 U.S.C. 112, as required under 119(e), and no priority is granted. Accordingly, priority under 35 U.S.C. 120 is set at the instant filing date, 5/07/02.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to the date recited above which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of, and fully enabled for, prior to that date.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The protein identified as PRO1926 is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises an "extracellular

domain" (for example see claim 1 parts (c) and (d)) is indefinite, as the art does not recognize soluble proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain"...."lacking its associated signal sequence" (claim 1, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

Rejections under 35 U.S.C. §101 and §112:

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8a. Claims 1-13 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The claims are directed to isolated polypeptides having at least 80% identity to SEQ DI NO: 134 with or without its signal peptide, or to the extracellular domain of SEQ DI NO: 134 with or without its signal peptide or the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC Accession NO: 203547. Finally, claims are presented to chimeric proteins comprising the aforementioned polypeptides. The specification contains numerous asserted utilities for the claimed polypeptides, including use to identify molecules that bind to PRO1926 (including agonists and antagonists), used diagnostically or therapeutically, as molecular weight markers, binding agents, and for the production of

antibodies. The utilities that pertain solely to polynucleotides (e.g. hybridization, chromosome and gene mapping, anti-sense) would not convey utility to the encoded protein. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO1926 protein, as each of the aforementioned utilities could be asserted for any naturally occurring protein, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO1926.

The specification asserts that PRO1926 is a secreted and transmembrane polypeptide. However, this family of proteins does not possess a common utility, but rather the proteins that can be broadly classified and have different activities, that confer different uses on them. Accordingly, the mere identification of a protein as belonging to a family, while indicative of evolutionary relatedness, is not indicative of function, nor by extension, of utility. The structure of the putative PRO1926 peptide is briefly discussed in Figure 136, as having a putative signal sequence, corresponding to amino acids 1-23 and a putative transmembrane domain around amino acids 161-182. Putative N-glycosylation site around amino acids 184-187 is identified. It also contends putative glycosaminoglycan attachment site is around amino acids 37-40 and 236-239. camp and cGMP-dependent protein kinase phosphorylation site is identified around amino acids 151-154. It also contends N-myristoylation sites are around amino acids 33-38, 36-41,38-44 and 229-234. Further it is described that there is a putative amidation site around amino acids 238-241. Finally, Applicants also describe a putative ATP/GTP-binding site motif A (P-loop). However, there is no functional characteristic associated with these motifs (domains), hence the mere observation that they exist is not probative

of function or utility. Further, there is no disclosure that the protein is expected to be a secreted protein, nor of any extracellular domain. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, any other specific feature that is disclosed as being associated with PRO1926. Without any information as to the specific properties of PRO1926, the mere identification of such as having homology to a secreted transmembrane protein is not sufficient to impart any particular utility to the claimed polypeptides.

The polynucleotide (cDNA) encoding PRO1926 is disclosed to highly express in normal esophagus compared to esophageal tumors based on the microarray analysis in Example 18 (see page 144, Table 7). Table 7 also describes that many other DNAs are over expressed in various tumors and normal tissues, based on which the specification made a general assertion that an over expressed protein in a diseased tissue is useful not only as a diagnosis marker for the presence of the disease condition, but also as a therapeutic target for treatment of the disease condition. The asserted utility in diagnosis and treatment is not substantial for the following reasons. The specification does not disclose the biological significance of this high or low expression levels, nor the correlation between the high/low expression of the DNA encoding protein PRO1926 and a predisposition to the onset of esophageal tumors, i.e., whether it is the cause or the result of the tumors. Further, there is no supporting evidence to indicate that the polypeptide encoded by the polynucleotide of the instant invention has higher or lower expression in tumor tissues compared to their normal tissue counterparts, and as such

one of skilled in the art would conclude that it is not supported by a substantial asserted utility or a well-established utility.

Although, the specification claims that the polynucleotide is more highly expressed in the normal esophagus, the specification does not teach what is the normal level of expression, does not indicate how high the expression level is compared to for example, esophageal tumors; and does not provide a statistical correlation to the level of expression (for example, there is no indication of how many samples were compared to study the expression). Furthermore, even if the tumor is malignant, the specification fails to describe the type or kind of tumor present in skin (for example, is it a sarcoma or adenocarcinoma etc.). Without knowing the identity of the tumors, one of skill in art cannot use the polynucleotides for diagnosis or therapeutic purposes as asserted. The specification does not disclose a correlation between any specific disorder and the altered level or form of the claimed polypeptides. In addition, the specification does not teach or describe the function of this yet to be identified polypeptide. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO1926 encoding polypeptides, as each of the aforementioned utilities could be asserted for any naturally occurring polypeptides, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO1926 polypeptides.

Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12: 82-88). The data presented in the instant specification are not corrected for aneuploidy. A higher amplification of a gene does not necessarily mean higher expression or lower expression in a tissue, but

can merely be an indication that the cancer tissue is aneuploid. The preliminary data were not supported by further analysis of mRNA or protein expression, for example. Also, the literature reports that it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased polypeptide expression, such that the claimed polypeptides would be useful for diagnosis of cancer or as a drug target. This fact is documented by Pennica et al. (1998, PNAS USA 95:14717-14722). In addition, they also observed that there was no correlation between WISP-2 mRNA expression and colon tumors. Furthermore they disclose that:

> "An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors." For example, WISP-2 RNA expression was significantly lower in the tumor than the mucosa (see p. 14721). Therefore, data pertaining to PRO1926 polyucleotides do not necessarily indicate anything significant regarding the claimed PRO1926 polypeptides. Thus, the data does not support the implicit assertion that the nucleotide encoding PRO1926 can be used in

cancer diagnosis or therapy. Significant further research would have been required of the skilled artisan to correlate the expression of PRO1926 in various disease and normal tissues to the extent that it could be used as a cancer diagnostic, and thus the implicitly asserted utility is not substantial.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed the polypeptides. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ: at 696.

A substantial utility, by definition, is a utility the defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not substantial utility. In the instant case, the higher expression of the nucleotides encoding PRO1926 in normal esophagus compared to esophageal tumors (if significant), at the most, is an interesting invitation for further research, experimentation and confirmation as to whether the PRO1926 is useful as a diagnosis marker, or suitable as a therapeutic target for treatment of the tumors. These further research and experimentation, however, is part of the act of invention, and until it has been undertaken, the claimed invention is not considered substantial.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9a. Claims 1-13 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further, *even if* the specification taught how to use the PRO1926 polypeptide, enablement would not be commensurate in scope with claims 1-6, 9, 10, 12 and 13, which encompass % variants of SEQ DI NO: 136 (claims 1-5, for example), and a fragment of the extracellular domain of SEQ DI NO: 136 (claims 1-6, 9 and 10 for example).

The specification discloses one PRO1926 amino acid sequence with particularity. No other PRO1926 variants or fragments comprising the sequence meeting the limitations of these claims were ever identified or particularly described. The specification does not teach how to make PRO1926 variants or fragments comprising the sequence. Since a biological function of PRO1926 is not clear, and since one skilled in the art could not determine with reasonable expectation of success what a biological function of PRO1926 would be, the skilled artisan would not be able to make PRO1926 variants or fragments comprising the sequence, and test them for biological activity. Furthermore, the specification provides no guidance as to how the skilled artisan could

use inactive PRO1926 variant or fragment, as no functional limitation associated with PRO1926 variants or fragments comprising the sequence in the claims.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Therefore, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope, because the skilled artisan would have no reasonable expectation of being able to make and use PRO1926 variants or fragments comprising the sequence for any purpose stated in the specification.

9b. Claims 1-6, 9, 10, 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The claims are drawn to polynucleotides having at least 80%, 85%, 95% or 99% sequence identity with a particular disclosed sequence. The claims do not require that the claimed polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. The specification teaches that PRO1926 has (unspecified) homology to secreted and transmembrane polypeptides. The structure of the putative PRO1926 peptide is briefly discussed in Figure 136, as having a putative signal sequence, corresponding to amino acids 1-23 and a putative transmembrane domain around amino acids 161-182. Putative N-glycosylation site around amino acids 184-187 is identified. It also contends putative glycosaminoglycan attachment site is around amino acids 37-40 and 236-239. camp and cGMP-dependent protein kinase phosphorylation site is identified around amino acids 151-154. It also contends N-myristoylation sites are around amino acids 33-38, 36-41,38-44 and 229-234. Further it is described that there is a putative amidation site around amino acids 238-241. Finally, Applicants also describe a putative ATP/GTP-binding site motif A (P-loop). However, there is no functional characteristic associated

with these motifs (domains), hence the mere observation that they exist is not probative of function or utility. Further, there is no disclosure that the protein is expected to be a transmembrane protein, nor of any extracellular domain.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1616.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the human sequence.

In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion

of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ DI NO: 134, with or without the signal sequence, but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10a. Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Valenzuela et al. (WO200055375A1)

Valenzuela et al. (WO200055375) disclose a 242 amino acids long sequence that has 100% identity to SEQ ID NO: 136 (see Appendix A). Thus, meeting the limitations of claims 1-11. It also describes fusion proteins with heterologous polypeptide such as maltose binding proteins (page 280, lines 25-30). In addition, the reference also teaches epitope tagging of the protein (page 280, lines 30-31), meeting

the limitations of claims 12 and 13. Therefore, claims 1-13 are rejected as being anticipated by Valenzuela et al. (WO200055375A1).

11. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 01/05

Brenda Brumback
BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice to Comply	Application No. 10/063661	Applicant(s) Eaton et al.
	Examiner J. Schwasegan	Art Unit 1647

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☑ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
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OM protein - protein search, using sw model

Run on: December 24, 2004, 17:53:58 ; Search time 287 Seconds
(without alignments)
302.483 Million cell updates/sec

Title: US-10-063-743-136
Perfect score: 1242
Sequence: 1 MAAALWGFFPVLLLLLLSGD.....SGKSSSGSSKTGKSGAGKRR 242

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2002273 seqs, 358729299 residues

Total number of hits satisfying chosen parameters: 2002273

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_23Sep04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1242	100.0	242	3	AAB34724	Aab34724 Human sec
2	1242	100.0	242	4	AAM23598	Aam23598 Human EST
3	1242	100.0	242	4	AAU29217	Aau29217 Human PRO
4	1242	100.0	242	4	AAB97078	Aab97078 Human hAR
5	1242	100.0	242	4	AAB87593	Aab87593 Human PRO
6	1242	100.0	242	5	ABG95918	Abg95918 Human sec
7	1242	100.0	242	6	ABU58593	Abu58593 Human PRO
8	1242	100.0	242	6	ABU88141	Abu88141 Novel hum
9	1242	100.0	242	6	ABU84456	Abu84456 Human sec
10	1242	100.0	242	6	ABR66330	Abr66330 Human sec
11	1242	100.0	242	6	ABR65720	Abr65720 Human sec
12	1242	100.0	242	6	ABU99660	Abu99660 Human sec
13	1242	100.0	242	6	ABU82899	Abu82899 Human PRO
14	1242	100.0	242	6	ABU90020	Abu90020 Novel hum
15	1242	100.0	242	6	ABR68269	Abr68269 Human sec
16	1242	100.0	242	6	ABJ37039	Abj37039 Human bre
17	1242	100.0	242	6	ABU96322	Abu96322 Novel hum
18	1242	100.0	242	6	ABU92753	Abu92753 Human sec
19	1242	100.0	242	6	ABO08830	Abo08830 Human sec
20	1242	100.0	242	6	ABO02882	Abo02882 Human sec
21	1242	100.0	242	6	ABR75036	Abr75036 Human sec
22	1242	100.0	242	6	ABR94798	Abr94798 Human sec
23	1242	100.0	242	6	ABU85771	Abu85771 Human PRO
24	1242	100.0	242	6	ABU98931	Abu98931 Novel hum
25	1242	100.0	242	6	ABU98146	Abu98146 Novel hum
26	1242	100.0	242	6	ABU91852	Abu91852 Novel hum
27	1242	100.0	242	6	ABU89545	Abu89545 Human PRO
28	1242	100.0	242	6	ABU86386	Abu86386 Human sec
29	1242	100.0	242	6	ABU67599	Abu67599 Human sec
30	1242	100.0	242	6	ABU80627	Abu80627 Human PRO
31	1242	100.0	242	6	ABU90943	Abu90943 Novel hum
32	1242	100.0	242	6	ABO34002	Abo34002 Human sec
33	1242	100.0	242	6	ABR99545	Abr99545 Human sec
34	1242	100.0	242	6	ABR98935	Abr98935 Human sec
35	1242	100.0	242	6	ABO16458	Abo16458 Human sec
36	1242	100.0	242	6	ABR92358	Abr92358 Human sec
37	1242	100.0	242	6	ABO18999	Abo18999 Human sec
38	1242	100.0	242	6	ABR78420	Abr78420 Human sec
39	1242	100.0	242	6	ABU72019	Abu72019 Novel hum
40	1242	100.0	242	6	ABU85156	Abu85156 Novel hum
41	1242	100.0	242	6	ABO00295	Abo00295 Novel hum
42	1242	100.0	242	6	ABO11627	Abo11627 Human sec
43	1242	100.0	242	6	ABO02272	Abo02272 Human sec
44	1242	100.0	242	6	ABU88846	Abu88846 Novel hum
45	1242	100.0	242	6	ABU83541	Abu83541 Human sec

ALIGNMENTS

RESULT 1
AAB34724
ID AAB34724 standard; protein; 242 AA.
XX
AC AAB34724;
XX
DT 26-JAN-2001 (first entry)
XX
DE Human secreted protein encoded by DNA clone vo25 1.
XX
KW Secreted protein; human; autoimmune disorder; multiple sclerosis; ulcer;
KW systemic lupus erythematosus; rheumatoid arthritis; anaemia; stroke;
KW haematopoiesis regulation; tissue regrowth; wound healing; haemophilia;
KW Alzheimer's disease; Parkinson's disease; Shy-drager syndrome; cancer;
KW contraceptive; infection; growth inhibition; hyperproliferative disorder;
KW psoriasis.
XX
OS Homo sapiens.
XX
PN WO200055375-A1.
XX
PD 21-SEP-2000.
XX
PF 17-MAR-2000; 2000WO-US007285.
XX
PR 17-MAR-1999; 99US-0124808P.
PR 17-MAR-1999; 99US-0124916P.
PR 17-AUG-1999; 99US-0149639P.
PR 01-OCT-1999; 99US-0157247P.
PR 29-NOV-1999; 99US-0167824P.
PR 15-FEB-2000; 2000US-0182711P.
XX
PA (ALPH-) ALPHAGENE INC.
XX
PI Valenzuela D, Yuan O, Hoffman H, Hall J, Rapiejko P;
XX
DR WPI; 2000-638211/61.
DR N-PSDB; AAC59825.
XX
PT Novel proteins and polypeptides useful for the treatment of e.g multiple
PT sclerosis, systemic lupus erythmatosus, rheumatoid arthritis, cancer,
PT Alzheimer's disease, Parkinson's disease, stroke, anemia and ulcers.
XX
PS Claim 84; Page 437-438; 493pp; English.
XX
CC This invention relates to 59 human secreted proteins and the nucleotide
CC sequences encoding them. Sequences AAC59788-C59846 and AAB34687-B34745
CC represent the proteins and their encoding nucleotide sequences, and

CC sequences AAB34746-B34771 represent fragments of the proteins. Probes for
CC the DNA sequences are represented by sequences AAC59847-C59596. The
CC proteins exhibit neuroprotective, dermatological, immunosuppressive,
CC antiinflammatory, antianaemic, nootropic, antiparkinsonian,
CC cerebroprotective, haemostatic, vulnerary, cytostatic, antipsoriatic,
CC antibacterial, virucide, and fungicide activity. The proteins and
CC nucleotide sequences are useful as nutritional sources or supplements and
CC in research. The proteins are useful for treating immune deficiency and
CC disorders, which may be genetic or resulting from infections, autoimmune
CC disorders such as multiple sclerosis, systemic lupus erythmatosus,
CC rheumatoid arthritis, and for treating myeloid or lymphoid cell
CC deficiencies such as anaemias by regulating haematopoiesis. The proteins
CC are also useful in compositions for bone, cartilage, tendon, ligament
CC and/or nerve tissue growth or regeneration, for wound healing, tissue
CC repair and replacement and in the treatment of wounds, incisions and
CC ulcers. Other uses include in the treatment of central and peripheral
CC nervous system and neuropathies such as Alzheimer's and Parkinson's
CC diseases and Shy-Drager syndrome, and mechanical and traumatic disorders,
CC such as spinal cord disorders, head trauma and stroke. The proteins may
CC also be used as a contraceptive, and for treating coagulation disorders
CC such as haemophilias. The protein and nucleotide sequences with cadherin
CC activity are useful for treating cancer. Other uses for the protein
CC include for inhibiting the growth, infection or function of, or killing,
CC infectious agents such as bacteria, virus, fungi and other parasites, for
CC effecting bodily characteristics such as height, weight, hair colour,
CC effecting biorhythms or cardiac cycles or rhythms, effecting metabolism,
CC catabolism, anabolism, processing, utilization, storage or elimination of
CC dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors,
CC effecting behavioural characteristics, providing analgesic effects and
CC for treating hyperproliferative disorders such as psoriasis
XX
SQ Sequence 242 AA;

Query Match 100.0%; Score 1242; DB 3; Length 242;
Best Local Similarity 100.0%; Pred. No. 5.6e-128;
Matches 242; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 MAAALWGFFPVLLLLLLSGDVQSSEVPGAAAEGSGGSGVGIGDRFKIEGRAVVPGVKPQD 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MAAALWGFFPVLLLLLLSGDVQSSEVPGAAAEGSGGSGVGIGDRFKIEGRAVVPGVKPQD 60

Qy         61 WISAARVLVDGEEHVGFLKTDGSFVVHDIPSGSYVVEVVSPAYRFDPVRVDITSKGKMRA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 WISAARVLVDGEEHVGFLKTDGSFVVHDIPSGSYVVEVVSPAYRFDPVRVDITSKGKMRA 120

Qy        121 RYVNYIKTSEVVRLPYPLQMKSSGPPSYFIKRESWGWTDFLMNPMVMMMVLPLLIFVLLP 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 RYVNYIKTSEVVRLPYPLQMKSSGPPSYFIKRESWGWTDFLMNPMVMMMVLPLLIFVLLP 180

Qy        181 KVVNTSDPDMRREMEQSMNMLNSNHELPDVSEFMTRLFSSKSSGKSSSGSSKTGKSGAGK 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 KVVNTSDPDMRREMEQSMNMLNSNHELPDVSEFMTRLFSSKSSGKSSSGSSKTGKSGAGK 240

Qy        241 RR 242
              ||
Db        241 RR 242
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RESULT 2
AAM23598
ID AAM23598 standard; protein; 242 AA.
XX
AC AAM23598;
XX
DT 12-OCT-2001 (first entry)
XX
DE Human EST encoded protein SEQ ID NO: 1123.
XX
KW Human; sheep; pig; cow; fruit fly; yeast; hamster; macaque; horse;
KW tomato; monkey; dog; sea urchin; expressed sequence tag; EST;
KW diagnostics; forensic test; gene mapping; genetic disorder; biodiversity;
KW gene therapy; nutrition.
XX

OS Homo sapiens.
XX
PN WO200154477-A2.
XX
PD 02-AUG-2001.
XX
PF 25-JAN-2001; 2001WO-US002687.
XX
PR 25-JAN-2000; 2000US-00491404.
PR 17-JUL-2000; 2000US-00617746.
PR 03-AUG-2000; 2000US-00631451.
PR 15-SEP-2000; 2000US-00663870.
XX
PA (HYSE-) HYSEQ INC.
XX
PI Tang YT, Liu C, Zhou P, Qian XB, Wang Z, Chen R, Asundi V;
PI Cao Y, Drmanac RA, Zhang J, Werhman T;
XX
DR WPI; 2001-476164/51.
DR N-PSDB; AAH98257.
XX
PT Isolated polypeptide for treatment of diseases, diagnostics, raising
PT antibodies and research use.
XX
PS Claim 20; Page 834-835; 1275pp; English.
XX
CC The present invention provides the protein and coding sequences of novel
CC proteins from a variety of organisms, including human, dog, cat, horse,
CC cow, pig, hamster, monkey, macaque, yeast, bacteria, fruit fly, sea
CC urchin and tomato. These were derived from expressed sequence tags (ESTs)
CC from the organism of interest. They can be used in diagnostics,
CC forensics, gene mapping, identification of mutations, to assess
CC biodiversity and for nutritional purposes. The present sequence is a
CC protein of the invention
XX
SQ Sequence 242 AA;

Query Match 100.0%; Score 1242; DB 4; Length 242;
Best Local Similarity 100.0%; Pred. No. 5.6e-128;
Matches 242; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 MAAALWGFFPVLLLLLLSGDVQSSEVPGAAAEGSGGSGVGIGDRFKIEGRAVVPGVKPQD 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MAAALWGFFPVLLLLLLSGDVQSSEVPGAAAEGSGGSGVGIGDRFKIEGRAVVPGVKPQD 60

Qy         61 WISAARVLVDGEEHVGFLKTDGSFVVHDIPSGSYVVEVVSPAYRFDPVRVDITSKGKMRA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 WISAARVLVDGEEHVGFLKTDGSFVVHDIPSGSYVVEVVSPAYRFDPVRVDITSKGKMRA 120

Qy        121 RYVNYIKTSEVVRLPYPLQMKSSGPPSYFIKRESWGWTDFLMNPMVMMMVLPLLIFVLLP 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 RYVNYIKTSEVVRLPYPLQMKSSGPPSYFIKRESWGWTDFLMNPMVMMMVLPLLIFVLLP 180

Qy        181 KVVNTSDPDMRREMEQSMNMLNSNHELPDVSEFMTRLFSSKSSGKSSSGSSKTGKSGAGK 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 KVVNTSDPDMRREMEQSMNMLNSNHELPDVSEFMTRLFSSKSSGKSSSGSSKTGKSGAGK 240

Qy        241 RR 242
              ||
Db        241 RR 242
```

RESULT 3
AAU29217
ID AAU29217 standard; protein; 242 AA.
XX
AC AAU29217;
XX
DT 18-DEC-2001 (first entry)
XX
DE Human PRO polypeptide sequence #194.
XX
KW PRO polypeptide; mammal; tumour; cancer; human; cattle; horse; sheep;